

**REMARKS**

Claims 1-36 were pending in the application. Claims 1-7, 9, 12-15, 17, 20-25, and 30-36 have been cancelled. Claims 1-7, 12-15, 20-25, and 30-36 have been cancelled for being withdrawn from consideration as being directed to a non-elected invention. Claims 8, 10-11, 16, 18-19, and 26-29 have been amended. New claims 37-39 have been added.

Support for the amendment to claims 8, 16, and 26 can be found in the specification at least at page 4, lines 12-13 and page 22, lines 23-26. Support for the amendment to claims 8 and 16 can also be found in the specification at page 8, line 28 to page 9, line 3 and in the claims as originally filed. Additional support for the amendment to claim 8 can be found in the specification at least at page 7, lines 14-21 and in Figure 9. Claims 10-11, 18-19, and 27-29 have been amended to correct for formalities. Support for new claims 37-39 can be found in the specification at page 4, lines 15-17, at page 4, line 29 to page 5, line 7, and in the claims as originally filed. No new matter has been added.

Amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

**Rejection of Claims Under 35 U.S.C. § 101**

Applicants gratefully acknowledge the Examiner's withdrawal of the rejection of claims 11, 19, and 29 under 35 U.S.C. § 101.

**Rejection of Claims 8-11, 16-19, 26, and 28-29 Under 35 U.S.C. § 112, Second Paragraph**

Applicants gratefully acknowledge the Examiner's withdrawal of the rejection of claims 8-11, 16-19, and 26-29 under 35 U.S.C. § 112, second paragraph.

*I. Rejection of Claims 8, 16, 26 Under 35 U.S.C. § 112, Second Paragraph*

The Examiner has rejected claims 8, 16, and 26 under 35 U.S.C. § 112, second paragraph for recitation of the phrase "active." The Examiner states that it is "a relative term from which no basis of comparison can be made."

Applicants respectfully traverse the foregoing rejection on the grounds that claims 8, 16, and 26 particularly point out and distinctly claim the subject matter which Applicants regard as their invention, as required by 35 U.S.C. § 112, second paragraph for the reasons stated in the response filed on February 13, 2003 and for those recited herein. Based on the plain language of the claims and the teachings in Applicants' specification, claims 8, 16, and 26 are clear and definite to one of ordinary skill in the art who would recognize that the term "active" is intended to mean a receptor-Ig-fusion protein which is biologically active as opposed to a receptor-Ig-fusion protein which is inactive or not biologically active.

Applicants provide working examples which delineate the difference between active and inactive receptor-Ig-fusion proteins. Applicants show that active and inactive (live and dead, respectively) receptor-Ig-fusion proteins have different sizes, determined by nonreducing SDS-PAGE analysis. As described in the specification at page 11, line 26 to page 12, line 3, Applicants explain that when purified receptor-Ig-fusion proteins are separated on a nonreducing gel, two forms of the protein, a higher weight form (a large form) and lower weight form (a small form), are evident. Applicants demonstrate that the large form of the receptor-Ig fusion protein is the biologically active form by showing that functional-specific antibodies only bind to the larger form. Applicants use FACs analysis to examine whether the large and small forms of the receptor-Ig-fusion protein can bind to cells expressing ligand (see results in Figure 5 of the specification). Applicants determine that only the large form is biologically active, because only the large form can bind ligand (see page 12, lines 10-15).

Applicants maintain that based on the teachings of the specification and the art-recognized use of the word, the term "active" is clear and definite to one of ordinary skill in the art. In the interest of expediting prosecution, however, Applicants have amended the claims to

specify a “*biologically* active” receptor-Ig-fusion protein. In view of this amendment, Applicants respectfully request that the rejection of claim 8, 16, and 26 under section 112 be reconsidered and withdrawn.

*II. Rejection of Claims 28-29 Under 35 U.S.C. § 112, Second Paragraph*

The Examiner has rejected claims 28-29 under 35 U.S.C. § 112, second paragraph for being indefinite in the recitation of the term "fragment." Applicants assert that "fragment" is a term of art that would be recognized by one of ordinary skill in the art and that the specification clearly supports use of the term. However, in view of the definition of the term receptor-Ig-fusion protein in the specification (see page 8, lines 25-28) and in the interest of expediting prosecution, Applicants have amended the claims to delete reference to the term "fragment," thus rendering the rejection moot.

*III. Rejection of Claims 8-11, 16-19 and 26-29 Under 35 U.S.C. § 112, Second Paragraph*

The Examiner has rejected claims 8-11, 16-19, and 26-29 under 35 U.S.C. § 112, second paragraph for recitation of the word "fusion." The Examiner states that use of the term "fusion" is unclear because it does not describe the type of fusion. Applicants have amended claims 8-11, 16-19, and 26-29 to specify that the fusion of the invention is a receptor-Ig-fusion protein. In view of this amendment, Applicants respectfully request that the Examiner withdraw the rejection.

Rejection of Claims 28 and 29 under 35 U.S.C. § 112, First Paragraph

Applicants gratefully acknowledge the Examiner's withdrawal of the rejection of claims 10, 11, 18, and 19 under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 28 and 29 under 35 U.S.C. § 112, first paragraph. The Examiner states that fragments of the LT- $\beta$  receptor are not described in the specification. Applicants respectfully traverse this rejection for the reasons stated above and those of record.

In the interest of expediting prosecution, however, Applicants have amended the claims to delete reference to the term "fragment," thus rendering the rejection moot.

Rejection of Claims 8-10 Under 35 U.S.C. §102(b)

The Examiner has rejected claims 8-10 as being anticipated by Crowe *et al.* (1994) *Science* 264:707 (hereinafter Crowe-Science) in view of Crowe *et al.* (1994) *J. Immunol. Methods* 168:79 (hereinafter Crowe-Immunol). Applicants have cancelled claim 9 and have amended claim 8 to describe a composition comprising at least 70% biologically active receptor-immunoglobulin-fusion protein (receptor-Ig-fusion protein) obtained by culturing a mammalian host cell transformed with DNA encoding the fusion in a culture system having a temperature of about 27° C to about 35 ° C, wherein the receptor-Ig fusion protein comprises a member of the TNF family of receptors.

Applicants submit that Crowe-Immunol does not teach or suggest a composition comprising at least 70% biologically active receptor Ig-fusion proteins, wherein the receptor Ig-fusion protein comprises a member of the TNF family of receptors. Crowe-Immunol describes a *lymphotoxin*-Fc fusion protein which is produced at a low temperature in *insect* cells, and does not teach culturing *mammalian* host cells to express a *receptor*-Ig-fusion protein. In addition, Crowe-Immunol does not teach or suggest a composition comprising **at least 70% biologically active** receptor Ig-fusion proteins, as required by amended claims 8-10. In view of the above amendments and the remarks herein, Applicants respectfully request that the rejection of claims 8-10 in view of Crowe-Immunol be withdrawn.

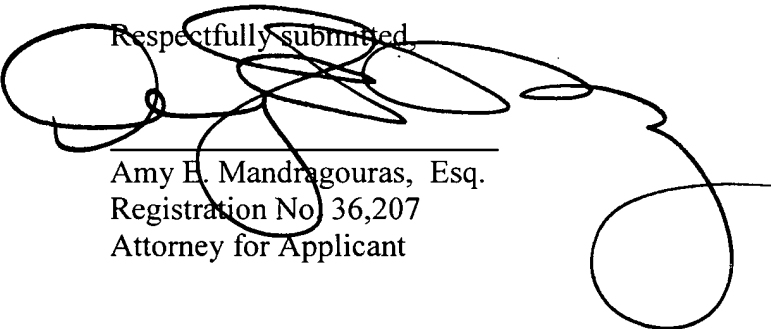
Crowe-Science does not teach or suggest a composition comprising **at least 70% biologically active** receptor-Ig-fusion protein obtained by culturing a mammalian host cell transformed with DNA encoding the fusion in a culture system having a temperature of **about 27° C to about 35 ° C**. The fusion proteins described in Crowe-Science were made according to standard culture conditions, *i.e.* 37° C (see Farlow *et al.* cited as reference 27 in Crowe *et al.* at page 709, column 3, no. 7). Applicants demonstrate that culturing cells at a temperature lower

(about 27° C to about 35 ° C) than that described by Crowe-Science, increases the amount of biologically active receptor-Ig-fusion protein (see Figure 9 of the specification). In fact, using conditions substantially similar to those described in Crowe-Science, Applicants show that incubating cells at standard temperatures, *e.g.*, 37 ° C results in a much higher percentage of biologically *inactive* receptor-Ig-fusion proteins. Thus, the standard culture conditions described in Crowe-Science would not result a composition comprising least 70% biologically active receptor-Ig-fusion protein as described in the claims. Accordingly, Applicants respectfully request that the Examiner withdraw the §102 rejection of claims 8-10.

### CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



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